

Amendments to the Specification:

Please replace paragraph [0083] with the following amended paragraph:

In certain preferred embodiments, the surfactant is selected from polyethylene glycol stearate, d- α -tocopheryl polyethylene glycol succinate, ~~poloxyl~~ polyoxyl stearate, ~~poloxyl~~ polyoxyl castor oil, a polyoxyethylene sorbitan fatty acid ester, a polyethylene glycol ether, a saturated polyglycolized glyceride, a fatty acid ester of polyethylene glycol, a hydroxylated lecithin, a medium chain monoglyceride, a medium chain fatty acid ester, and polyethylene-propylene glycol copolymer. In other preferred embodiments, the lipid is a diester of coconut fatty acids and propylene glycol. In other preferred embodiments, the organic solvent is selected from propylene glycol, propylene carbonate, dimethyl isosorbide, and polyethylene glycol (PEG). In other preferred embodiments, the antioxidant is selected from ascorbic acid, a fatty acid ester of ascorbic acid, and butylated hydroxyanisole.

Please replace paragraph [0111] with the following amended paragraph:

Surfactants include, but are not limited to, polyoxyethylene stearates, polyoxyethylene castor oil, polyoxyethylene sorbitan fatty acid esters (sorbitans), polyethylene glycol ethers, saturated polyglycolized glycerides, fatty acid esters of polyethylene glycol, hydroxylated lecithins, medium chain monoglycerides, medium chain fatty acid esters, polyethylene/propylene glycol copolymers, polyethylene glycol stearate, d- α -tocopheryl polyethylene glycol succinate, ~~poloxyl~~ polyoxyl stearate (e.g., Myrj[®] 52) and ~~poloxyl~~ polyoxyl castor oil.

Please replace paragraph [0139] with the following amended paragraph:

Preferred heterocyclic groups formed with a nitrogen atom include pyrrolidinyl, piperidinyl, piperidino, morpholinyl, morpholino, thiomorpholino, N-methylpiperazinyl, indolyl, isoindolyl, imidazole, imidazoline, oxazoline, oxazole, triazole, thiazoline, thiazole, isothiazole, thiadiazoles, triazines, isoxazole, oxindole, indoxyl, pyrazole, pyrazolone, pyrimidine, pyrazine, quinoline, ~~isoquinoline~~ isoquinoline, and tetrazole groups. Preferred heterocyclic groups formed with an oxygen atom include furan, tetrahydrofuran, pyran, benzofurans, isobenzofurans, and tetrahydropyran groups. Preferred heterocyclic groups formed with a sulfur atom include thiophene, thianaphthene, tetrahydrothiophene, tetrahydrothiapyran, and benzothiophenes.

Please replace paragraph [0147] with the following amended paragraph:

The fused pyrrolocarbazole may be present in various forms as will be appreciated by the skilled artisan. Such forms include, but are not limited to, pharmaceutically acceptable salts, prodrugs, polymorphs, stereoisomers, and the like. As used herein, the term "pharmaceutically acceptable" refers to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem complications commensurate with a reasonable benefit/risk ~~ration~~ ratio.

Please replace paragraph [0155] with the following amended paragraph:

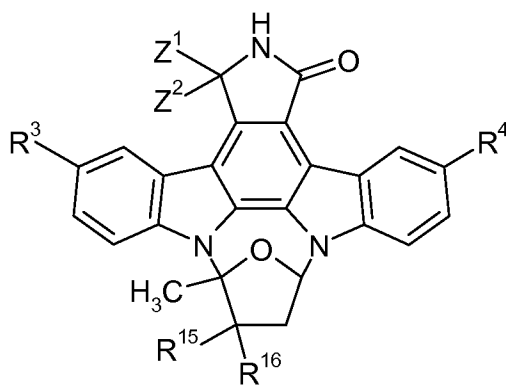
Fused pyrrolocarbazoles, such as indolocarbazoles may be synthesized by methods taught, for example, in U.S. Patent

Nos. 4,923,986; 4,877,776; 5,093,330; 5,461,146; 5,468,872; 5,621,100; 5,621,101; 5,516,771; and 5,599,808; and PCT publication Nos. WO 93/08809 and WO 97/46565, the ~~discloses~~ disclosures of which are hereby incorporated herein by reference in their entirety. Additional methods of preparation are set forth in Moody et al., *J. Org. Chem.* 57:2105-2114 (1992), also incorporated herein by reference.

Please replace paragraph [0158] with the following amended paragraph

The fused pyrrolocarbazoles disclosed in all foregoing references are contemplated for use in the particle-forming compositions of the present invention. Other exemplary fused pyrrolocarbazoles are the indolocarbazoles set forth in Tables I-A and I-B, wherein each entry corresponds to the accompanying structure.

Table I-A



II-a

Compound	R ⁴	R ³	R ¹⁵	R ¹⁶	Z ¹ ; Z ²
IIa-1	H	H	CH ₂ N ₃	OH	H; H
IIa-2	NHCONHC ₆ H ₅	H	CO ₂ CH ₃	OH	H; H
IIa-3	CH ₂ SOC ₂ H ₅	H	CO ₂ CH ₃	OH	H; H

DOCKET NO.: CP185B
Application No.: 10/718,077
Office Action Dated: January 6, 2009

PATENT

IIa-4	H	H	CH ₂ OH	OCH ₃	H;H
IIa-5	H	H	CONHC ₂ H ₅	OH	H;H
IIa-6	H	H	CH=NNH-2- imidazoline	OH	H;H
IIa-7	H	H	CH ₂ NH-Gly	OH	H;H
IIa-8	H	H	CON(CH ₃) ₂	OH	H;H
IIa-9	H	H	-CH ₂ NHCO ₂ -	(with X)	H;H
IIa-10	Br	H	CO ₂ CH ₃	OH	H;H
IIa-11	H	H	CONH ₂	OH	H;H
IIa-12	H	H	CH ₂ OH	OH	H;H
IIa-13	H	H	CONHC ₃ H ₇	OH	H;H
IIa-14	H	H	CH ₂ NH-Serine	OH	H;H
IIa-15	H	H	CH ₂ SOCH ₃	OH	H;H
IIa-16	H	H	CH=NOH	OH	H;H
IIa-17	H	H	CON-morpholine	OH	H;H
IIa-18	H	H	CH ₂ NH-Proline	OH	H;H
IIa-19	H	H	CH=NNHC(=NH)NH ₂	OH	H;H
IIa-20	Br	Br	CO ₂ CH ₃	OH	=O
IIa-21	H	H	CONH(CH ₂) ₂ OH	OH	H;H
IIa-22	H	H	CO ₂ CH ₃	OH	=O
IIa-23	H	H	H	OH	H;H
IIa-24	H	H	CH=NNHCONH ₂	OH	H;H
IIa-25	H	H	CH ₂ OCOCH ₃	OH	H;H
IIa-26	H	H	-CH ₂ OC(CH ₃) ₂ O-	(with X)	H;H
IIa-29	NHCONHC ₂ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-30	CH ₂ SC ₂ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-31	Br	H	CH ₂ OH	OH	H;H
IIa-32	Br	Br	CO ₂ CH ₃	OH	H;H
IIa-33	CH ₂ SC ₆ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-34	Cl	Cl	CO ₂ CH ₃	OH	H;H

IIa-36	H	H	CONHC ₆ H ₅	OH	H;H
IIa-37	H	H	CH ₂ SO	OH	H;H
IIa-38	H	H	CH ₂ NHCO ₂ C ₆ H ₅	OH	H;H
IIa-39	NHCONHC ₂ H ₅	NHCONHC ₂ H ₅	CO ₂ CH ₃	OH	H;H
IIa-40	N(CH ₃) ₂	H	CO ₂ CH ₃	OH	H;H
IIa-41	CH ₃	H	CO ₂ CH ₃	OH	H;H
IIa-42	CH ₂ OCONHC ₂ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-43	NHCO ₂ CH ₃	H	CO ₂ CH ₃	OH	H;H
IIa-44	Br	Br	CH ₂ OH	OH	H;H
IIa-45	Br	Br	CONHC ₆ H ₅	OH	H;H
IIa-46	Br	Br	CONHCH ₂ CH ₂ OH	OH	H;H
IIa-47	CH ₂ OC ₂ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-48	CH ₂ N(CH ₃) ₂	H	CO ₂ CH ₃	OH	H;H
IIa-49	CH ₂ SO ₂ C ₂ H ₅	H	CO ₂ CH ₃	OH	H;H
IIa-50	CH ₂ S	H	CO ₂ CH ₃	OH	H;H
IIa-51	CH ₂ SC ₂ H ₅	CH ₂ SC ₂ H ₅	CO ₂ CH ₃	OH <u>OMe</u>	H;H
IIa-52	CH=NNH	H	CO ₂ CH ₃	OH	H;H
IIa-53	CH ₂ S	H	CO ₂ CH ₃	OH	H;H
IIa-54	CH ₂ S(O)	H	CO ₂ CH ₃	OH	H;H
IIa-55	CH ₂ S(O)	H	CO ₂ CH ₃	OH	H;H
IIa-56	CH ₂ SC ₂ H ₅	CH ₂ OH	CO ₂ CH ₃	OH	H;H
IIa-57	H	H	CH ₂ NHCO ₂ CH ₃	OH	H;H
IIa-58	Br	H	CONH ₂	OH	H;H
IIa-59	H	H	CH ₂ SC ₆ H ₅	OH	H;H
IIa-60	H	H	CH ₂ S-2-pyridyl	OH	H;H
IIa-61	H	H	CH ₂ SOC ₆ H ₅	OH	H;H

Please replace paragraph [0174] with the following amended paragraph:

Numerous particle-forming compositions according to the invention have been formulated using various components in various amounts relative to one another. The formulations for

several particle-forming compositions are presented in Table 2, below.

Table 2

Exemplary Formulations

Form No.	Component (category)	Component (specific)	Amount	Solid/Liq (room temp)
1	indolocarbazole organic solvent surfactant	Compound IIa-51 PEG 1450 Poloxamer 188	100 mg/ml 70% 30%	solid
2	indolocarbazole organic solvent surfactant	Compound IIa-51 PEG 400 polysorbate 80	100 mg/ml 70% 30%	liquid
3	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-51 PEG 1450 propylene glycol Poloxamer 188	100 mg/ml 60% 20% 20%	solid
4	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-51 PEG 400 propylene glycol polysorbate 80	25 mg/ml 25% 25% 50%	liquid
5	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-51 PEG 400 propylene carbonate polysorbate 80	5 mg/ml 25% 25% 50%	liquid
6	indolocarbazole organic solvent surfactant surfactant	Compound IIa-51 Propylene glycol glyceryl monocaprylate Poloxamer 188	5 mg/ml 47.5% 47.5% 5%	liquid

Form No.	Component (category)	Component (specific)	Amount	Solid/Liq (room temp)
7	indolocarbazole organic solvent surfactant surfactant	Compound IIa-51 propylene glycol glyceryl monocaprylate polysorbate 80	25 mg/ml 25% 25% 50%	liquid
8	indolocarbazole organic solvent surfactant surfactant	Compound IIa-51 propylene glycol glyceryl monocaprylate glyceryl caprylate- caprate	1 mg/ml 40% 30% 30%	liquid
9	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-51 propylene glycol propylene carbonate polysorbate 80	50mg/ml 50% 25% 25%	liquid
10	indolocarbazole surfactant	Compound IIa-51 glyceryl monocaprylate	100 mg/ml 100%	solid
11	indolocarbazole surfactant surfactant	Compound IIa-51 glyceryl monocaprylate Poloxamer 188	100 mg/ml 70% 30%	solid
12	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol Gelucire <u>Gelucire®</u> 44/14	25 mg/ml 40% 60%	solid
13	indolocarbazole organic solvent lipid surfactant surfactant	Compound IIa-12 propylene glycol Captex <u>Captex®</u> 200 Capmul <u>Capmul®</u> MCM C-8 polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid

Form No.	Component (category)	Component (specific)	Amount	Solid/Liq (room temp)
14	indolocarbazole organic solvent lipid surfactant surfactant	Compound IIa-12 propylene glycol Captex ⁷ <u>Captex</u> [®] 200 Centrolene ⁷ <u>Centrolene</u> [®] A polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid
15	indolocarbazole organic solvent lipid surfactant surfactant	Compound IIa-12 propylene glycol Captex ⁷ <u>Captex</u> [®] 200 Imwitor ⁷ <u>Imwitor</u> [®] 308 polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid
16	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol polysorbate 80	25 mg/ml 50% 50%	liquid
17	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol Gelucire ⁷ 44/14	16.7mg/ml 10% 90%	solid
18	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-12 propylene glycol propylene carbonate polysorbate 80	25 mg/ml 10% 40% 50%	liquid
19	indolocarbazole organic solvent organic solvent surfactant	Compound IIa-12 propylene glycol dimethyl- isosorbide polysorbate 80	25 mg/ml 10% 40% 50%	liquid
20	indolocarbazole surfactant	Compound IIa-12 Gelucire ⁷ <u>Gelucire</u> [®] 44/14	15 mg/ml 100%	solid
21	indolocarbazole organic solvent surfactant	Compound IIa-51 propylene glycol Gelucire ⁷ <u>Gelucire</u> [®] 44/14	1 mg/ml 25% 75%	solid

Form No.	Component (category)	Component (specific)	Amount	Solid/Liq (room temp)
22	indolocarbazole surfactant	Compound IIa-51 Gelucire <u>Gelucire</u> ® 44/14	100 mg/ml 100%	solid
23	indolocarbazole surfactant surfactant	Compound IIa-51 Poloxamer 184 Capmul <u>Capmul</u> ® MCM	12 mg/ml 90% 10%	liquid

Please replace paragraph [0179] with the following amended paragraph:

Male Sprague-Dawley rats were given either a bolus i.v. dose administered into the tail vein, or p.o. doses by gavage in one of three formulations. The formulations were as described in Table 2A, below. Formulation (a) is not a particle-forming composition.

Table 2A

Formulations in Rat Study

Form.	Component (category)	Component (specific)	Amount	Solid/Liq. (room temp.)
(a)	indolocarbazole organic solvent organic solvent organic solvent water	Compound IIa-12 PEG 1000 PVP C30 benzyl alcohol water	5 mg/ml 40% 10% 2% 48%	liquid
(b)	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol Gelucire <u>Gelucire</u> ® 44/14	5 mg/ml 25% 75%	solid

Form.	Component (category)	Component (specific)	Amount	Solid/Liq. (room temp.)
(c)	indolocarbazole organic solvent surfactant surfactant surfactant	Compound IIa-12 propylene glycol Capmul 7 <u>Capmul®</u> MCM C-8 Captex 7 <u>Captex®</u> Polysorbate 80	5 mg/ml 30% 11% 14% 45%	liquid

Please replace paragraph [0187] with the following amended paragraph:

Each formulation (capsule or liquid) was administered to a group of three dogs, in a dose of 50 mg. The formulations were as described in Table 4, below. Formulations C and D are not particle-forming compositions.

Table 4
Formulations in Dog Study

Form	Component (category)	Component (specific)	Amount	Solid/Liq. (room temp)
A	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol Gelucire 7 <u>Gelucire®</u>	25 mg/ml 40% 60%	semi-solid w/out capsule
B	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol Gelucire 7 <u>Gelucire®</u>	25 mg/ml 40% 60%	semi-solid in capsule
C	indolocarbazole other surfactant	Compound IIa-12 croscarmellose SDS	50 mg/ml 5 mg 5 mg	solid in capsule
D	indolocarbazole organic solvent organic solvent water	Compound IIa-12 PEG 1000 sorbitol water	50 mg/ml 70% 21% 9%	solid in capsule
E	indolocarbazole organic solvent surfactant surfactant surfactant	Compound IIa-12 propylene glycol Captex 7 <u>Captex®</u> 200 Capmul 7 <u>Capmul®</u> MCM polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid

Form	Component (category)	Component (specific)	Amount	Solid/Liq. (room temp)
F	indolocarbazole organic solvent lipid surfactant surfactant	Compound IIa-12 propylene glycol Captex 7 <u>Captex®</u> 200 Centrolene A polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid
G	indolocarbazole organic solvent surfactant surfactant surfactant	Compound IIa-12 propylene glycol Captex 7 <u>Captex®</u> 200 Imwitor 7 <u>Imwitor®</u> 308 polysorbate 80	25 mg/ml 30% 14% 11% 45%	liquid
H	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol polysorbate 80	25 mg/ml 50% 50%	liquid
I	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol poloxyl <u>polyoxyl</u> 40 stearate	25 mg/ml 10% 90%	solid
J	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol poloxyl <u>polyoxyl</u> 35 castor oil	25 mg/ml 10% 90%	liquid
K	indolocarbazole organic solvent surfactant	Compound IIa-12 polyethylene glycol 1450 poloxamer 188	25 mg/ml 70% 30%	solid
L	indolocarbazole organic solvent surfactant	Compound IIa-12 polyethylene glycol 400 poloxyl <u>polyoxyl</u> 40 stearate	25 mg/ml 50% 50%	solid
M	indolocarbazole organic solvent surfactant	Compound IIa-12 propylene glycol polysorbate 80	25 mg/ml 50% 50%	liquid

Please replace paragraph [0194] with the following amended paragraph:

A bioavailability study involving Compound IIa-51 formulated in non-aqueous, particle forming compositions was carried out using monkeys. Pharmacokinetic parameters were

measured following intravenous (i.v.) administration and oral (p.o.) administration. The test composition consisted of four male cynomolgus monkeys. The i.v. dose was administered as a bolus, at a dosage level of 3 mg/kg. The oral doses were administered as soft gelatin capsules, at a dosage level of 10 mg/kg (2 capsules/monkey/dose). The oral formulations were as described in Table 6, below.

Table 6

Formulations in Monkey Study

Formula	Component (category)	Component (specific)	Amount	Solid/Liq. (room temp.)
A	indolocarbazole surfactant	Compound IIa-51 Imwitor ⁷ <u>Imwitor</u> [®] 308	20 mg/ml 100%	solid
B	indolocarbazole surfactant surfactant	Compound IIa-51 Imwitor ⁷ <u>Imwitor</u> [®] 308 Pluronic ⁷ <u>Pluronic</u> [®] F68	20 mg/ml 70% 30%	solid
C	indolocarbazole surfactant surfactant organic solvent	Compound IIa-51 Imwitor ⁷ <u>Imwitor</u> [®] 308 Pluronic ⁷ <u>Pluronic</u> [®] F68 propylene glycol	20 mg/ml 70% 20% 10%	solid
D	indolocarbazole organic solvent surfactant	Compound IIa-51 PEG1450 Pluronic ⁷ <u>Pluronic</u> [®] F68	20 mg/ml 70% 30%	solid